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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,018	11/03/2003	Paul M. Lizardi	25006.0003U4	4956

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EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,018	LIZARDI, PAUL M.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,34-44 and 46-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32, 34-44 and 46-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The applicant's response filed 10/31/07 to the office action has been entered. Claims 32, 34-44 and 46-55 are pending.

1. Claims 34, 39-44, 47-48, and 52-55 are rejected under 35 U.S.C. 102(e) as being anticipated by Lupski et al. (5,691,136, issued Nov. 1997) as evidenced by New England BioLabs catalogue.

Lupski et al. disclose oligonucleotide primers and a method for identifying strains of bacteria in a sample (See column 2, lines 27-30). The primers are about 10-29 nucleotide bases in length and preferably between about 15-25 bases in length (See column 3, lines 12-15). Each primer pair is selected to be substantially complementary to the different strands of each specific repetitive sequence to which the primer pairs bind (See column 5, lines 15-22). The sample contains a plurality of strains of bacteria (See column 6, lines 14-16, column 51, lines 65-67). The polymerases used in the method are *Taq* DNA polymerase, *E. coli* DNA polymerase I and Klenow fragment of *E. coli* DNA polymerase I and Vent DNA polymerase (See column 7, lines 17-24). The invention also includes a kit for the method containing a pair of PCR primers to a repetitive sequence in bacteria (See column 9, lines 29-33).

Lupski et al. do not explicitly disclose that each primer has a constant portion and a random portion.

In fig. 3, there are four primers in a right set and a left set. These sequences are the alignment of ERIC oligonucleotide primer sequences with respect to the central inverted repeat of an ERIC consensus sequence (See column 3, lines 51-54). It is inherent in this teaching that all of the primers in the set of primers are complementary to the same strand of the target

sequence as recited in claim 47. These primers are all of the same length (See fig. 3). There are four primers for a right set and a left set (See fig. 3) and the right set and left set of primers each has the same number of primers (See fig.3). The primers have a constant portion, TT, GGG, and AA (See fig. 3) and a random portion comprises ATCG (See fig. 2). The constant portion of each primer is the same (See fig. 3). Thus, Lupski et al. inherently teach that each primer has a constant portion and a random portion and the constant portion of each primer are the same.

Lupski et al. also do not disclose strand displacement factor compatible with DNA polymerase.

New England BioLabs disclose that Klenow fragment of *E. coli* DNA polymerase I has strand displacement activity (See attached New England BioLabs catalogue pages). It is inherent that the polymerase used by Lupski et al. has strand displacement activity.

Based upon the analysis above, the teachings of Lupski et al. anticipate the limitations of the claims.

The response argues that Lupski et al. does not explicitly disclose that each primer has a constant portion and a random portion. However, Lupski et al. disclose that the primers have a constant portion, TT, GGG, and AA (See fig. 3) and a random portion "ATCG" (See fig. 2 as "NCTA" in REP1R-Dt and N can be G, C, T or A). Nevertheless, there is no definition regarding "constant portion" and "random portion". The teachings of Lupski et al. satisfy the limitation. The response also indicates that the sequence "ATCG" is not present in any of the sequences shown in Fig. 3. This was an error in the Office action mailed 8/8/07 and the sequence "ATCG" is in fig. 2 as noted above.

The response argues that Lupski et al. fails to teach that the constant portion of each primer has the same nucleotide sequence. However, each primer as listed in fig. 3 has a constant portion, GGG and a random portion TN in which N can be G,C,T or A. The response specifically indicates that the ERIC1 and ERIC2 primers do not comprise the same sequence for each primer. However, Lupski et al. disclose that the sequence GGG is in the ERIC1 and the ERIC2 primer (See fig. 3). The teachings of Lupski et al. satisfy the limitation.

The response also argues that Lupski et al. do not disclose that the complementary portions of the primers are each complementary to a different portion of the hybridization target. However, Lupski et al. disclose that a variety of primers can be used to detect repetitive sequence in bacteria (See column 8, lines 20-21), a plurality of pairs of primers can be added to the method, each pair of primers will bind to a different repetitive sequence, for example, any combination of two or more of each of REP, ERIC, Ngrep and Drrep primer pairs can be added (See column 8, lines 65-67, column 9, lines 1-2), fig.1 shows the binding of outwardly-directed primers (See column 3, lines 46-47) which indicates that on one target there would be different primer binding sites and fig. 4 shows PCR amplification of *E.coli* strand W3110 genomic DNA with different REP and ERIC oligonucleotide sets (See column 3, lines 51-53). These inherently teach that the complementary portions of the primers are each complementary to a different portion of the hybridization target.

Based upon the discussion of the issues set forth above, the rejection is maintained.

2. Claims 32, 35-37, 49, and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lupski et al. (5,691,136, issued Nov. 1997).

Lupski et al. disclose oligonucleotide primers and a method for identifying strains of bacteria in a sample (See column 2, lines 27-30). The primers are about 10-29 nucleotide bases in length and preferably between about 15-25 bases in length (See column 3, lines 12-15). The method applies multiple primers to different repetitive DNA (See column 3, lines 30-34). Each primer pair is selected to be substantially complementary to the different strands of each specific repetitive sequence to which the primer pairs bind (See column 5, lines 15-22). The polymerases used in the method are *Taq* DNA polymerase, *E. coli* DNA polymerase I and Klenow fragment of *E. coli* DNA polymerase I and Vent DNA polymerase (See column 7, lines 17-24). The invention also includes a kit for the method containing a pair of PCR primers to a repetitive sequence in bacteria (See column 9, lines 29-33). The kit can have any of the PCR primers as disclosed by the invention (See column 9, lines 33-35). One skilled in the art will readily recognize that the number and type of primers, which are in the kit, will depend on the use of the kit as well as the sequences, which are to be detected (See column 9, lines 36-39). The sample contains a plurality of strains of bacteria (See column 51, lines 65-67).

Lupski et al. also do not disclose strand displacement factor compatible with DNA polymerase.

New England BioLabs disclose that Klenow fragment of *E. coli* DNA polymerase I has strand displacement activity (See attached New England BioLabs catalogue pages). It is inherent that the polymerase used by Lupski et al. has strand displacement activity.

Lupski et al. do not disclose that the kit contains 4 or more primers, which are respectively in a right set of primers, and a left set of primers.

In fig. 3, there are four primers in a right set and a left set. These sequences are the alignment of ERIC oligonucleotide primer sequences with respect to the central inverted repeat of an ERIC consensus sequence (See column 3, lines 51-54). These primers are all of the same length (See fig. 3). There are four primers for a right set and a left set (See fig. 3) and the right set and left set of primers each has the same number of primers (See fig.3). As indicated by Lupski et al., one skilled in the art would have readily recognized that the number and type of primers, which are in the kit, will depend on the use of the kit as well as the sequences, which are to be detected (See column 9, lines 36-39).

Thus one of ordinary skill in the art would have been motivated to make the kit with four or more primers in a right primer set and a left primer set because of the suggestion of Lupski et al. (See column 9, lines 36-39). It would have been prima facie obvious to make the kit with four or more primers, which are respectively in a right set and a left set.

The response argues that the method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17). However, fig.1 shows the binding of outwardly-directed primers (See column 3, lines 46-47) which indicates that on one target there would be different primer binding sites and fig. 4 shows PCR amplification of *E.coli* strand W3110 genomic DNA with different REP and ERIC oligonucleotide sets (See column 3, lines 51-53). This is an inherent teaching that the complementary portions of the primers are each complementary to a different portion of the hybridization target.

The response also argues that for example, each of the ERIC 1 primers in Figure 3 binds to the same portion of the ERIC consensus sequence while the ERIC2 primers in Figure 3 binds to the same portion of the complement of the ERIC consensus sequence. Nowhere in Lupski et al. is any other orientation of primers taught or suggested. The Office Action's reliance on Figure 3 for teaching or suggesting such a limitation is therefore incorrect. The argument of the response is correct, but as discussed above, fig.1 shows the binding of outwardly-directed primers (See column 3, lines 46-47) which indicates that on one target there would be different primer binding sites and fig. 4 shows PCR amplification of *E.coli* strand W3110 genomic DNA with different REP and ERIC oligonucleotide sets (See column 3, lines 51-53). It is inherent in these teachings that the complementary portions of the primers are each complementary to a different portion of the hybridization target.

The response argues that Lupski et al. do not provide motivation for one of skill in the art to choose the number of primers for a kit. However, Lupski et al. disclose that one skilled in the art would have readily recognized that the number and type of primers, which are in the kit, will depend on the use of the kit as well as the sequences which are to be detected (See column 9, lines 36-39). Therefore, this was a motivation for one of skill in the art to include a certain amount of primers as needed in a kit for conveniently performing a method.

Based upon the discussion of the issues set forth above, the rejection is maintained.

3. Claims 38, 46, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lupski et al. (5,691,136, issued Nov. 1997) as applied to claims 32, 34-37, 39-44, 47-49 and 52-

55 further in view of Blanco et al. (Journal of Biological Chemistry, 1989, Vol. 264(15), pg. 8935-40).

Lupski et al. do not disclose that the kit contains phage vphi 29 DNA polymerase for strand displacement activity.

Blanco et al. disclose that phage vphi 29 DNA polymerase is highly processive in the absence of any accessory protein and is able to produce strand displacement coupled to the polymerization process (See the Abstract).

One of ordinary skill in the art would have been motivated to include phage vphi 29 DNA polymerase in the kit for amplifying a target nucleic acid as claimed because of the benefit of using the vphi29 DNA polymerase. It would have been prima facie obvious to include phage vphi 29 DNA polymerase in the kit for performing the amplification of the target nucleic acid.

Since the response argues the same issues as argued in the 102(e) rejection and the 103 rejection as set forth above, with the same reasons as set forth above, the rejection is maintained.

Summary

4. No claims are allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung
January 11, 2008

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
1/17/08